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IMPACT OF DIABETIC NEPHROPATHY AND ANGIOTENSIN II RECEPTOR BLOCKADE ON URINARY POLY-PEPTIDE PATTERNS

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New insights into the pathogenesis and treatment of diabetic renal disease may emerge from recent advances in proteomics using high-throughput mass spectrometry (MS) of urine.

Using a combination of online capillary electrophoresis(CE) and MS we evaluated urinary polypeptide patterns(UPP) in 4 groups of type 2 diabetic patients matched for age, gender and diabetes duration including; 20 normoalbuminuric patients with and 20 without diabetic retinopathy(DR), 20 microalbuminuric patients with DR and 18 macroalbuminuric patients with DR. Furthermore, changes in UPP during treatment with the angiotensin II receptor blocker candesartan were evaluated in the macroalbuminuric patients in a randomized double-blind, cross-over trial where each patient received treatment with placebo, candesartan 8, 16 and 32 mg daily each for two months.

Overall 4551 different polypeptides were found in the samples. UPPs were comparable in normo- (with and without DR) and microalbuminuric patients whereas distinct differences were found in macroalbuminuric patients. Differences in UPP between normo- and macroalbuminuric patients permitted the establishment of a "diabetic renal damage" (DRD) pattern consisting of 113 polypeptides. Eleven of these polypeptides had been sequenced and identified. Candesartan treatment in macroalbuminuric patients significantly changed 15 of the 113 polypeptides in the DRD pattern towards levels in normoalbuminuric patients. Change in the DRD pattern was not candesartan dose-dependent but individual changes correlated with changes in urinary albumin excretion at each dose level. Additional studies to evaluate the predictive value of these polypeptides utilizing samples from longitudinal studies are underway and will be presented as well.

CE-MS serves as a fast and sensitive tool for identification of biomarkers. Urinary polypeptide patterns specific for macroalbuminuric type 2 diabetic patients may be used to explore and monitor renoprotective effects of angiotensin II receptor blockade as well as other therapeutic strategies.

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